

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Brenda F. Baker, et al.** Confirmation No.: **5280**
Serial No.: **10/701,236** Group Art Unit: **1635**
Filing Date: **November 4, 2003** Examiner: **Kimberly Chong**
For: **Sugar Surrogate-Containing Oligomeric Compounds and Compositions For Use In Gene Modulation**

APPELLANTS' REPLY BRIEF PURSUANT TO 37 C.F.R. § 41.41

This reply brief is being filed in response to the Examiner's Answer dated June 20, 2012. Since this reply brief is being filed on or before August 20, 2012, it is timely. For the reasons set forth in appellants' Appeal Brief filed on April 4, 2012, and those set forth below, the examiner's rejection is in error and should be reversed.¹

The Examiner Continues to Rely Upon Improper Hindsight

As previously discussed, the pending obviousness rejection can be aptly characterized as a "concept" rejection. Appeal Brief at 4-5. The examiner repeated the rejection from the non-final office action of June 22, 2010, when it was first made. Thus, the examiner once again does not start with a prior art composition that comprises a duplex consisting of a first and a second chemically synthesized oligonucleotide and propose changes to that core structure based upon teachings from the prior art. Rather, the examiner first constructs a *hypothetical* duplex from assorted teachings of Wyatt, Monia and Manche as follows:

Based on the teachings of Wyatt et al., Mania et al. and Manche et al., the person of ordinary skill would have reason to make short duplex oligonucleotides containing RNA residues and modified nucleotides for the purpose of studying enzyme structure and activity and would recognize that these duplexes could be made of various

¹ The examiner lists a reference to "Inoue et al." as "Evidence Relied Upon" at page 4 of the Examiner's Answer. However, the examiner has not relied upon Inoue in rejecting the pending claims. Thus, the listing of Inoue is seen to be an inadvertent mistake.

lengths, depending on the requirements of the particular enzyme being studied, for example, Mania et al. provide an explicit teaching of an artificial enzyme substrate comprising 17 and 25 [linked] nucleotide[s]....

Examiner's Answer at 7. Then the examiner proposes to modify this *hypothetical* duplex based upon additional teachings of Monia and Baracchini, stating:

Based on the teachings of Mania [sic] et al. and Baracchini et al, the person of ordinary skill in the art would have reason to incorporate 2'-sugar groups into the duplex because these references teach that nucleolytic degradation is a problem for nucleic acids and that stabilization of a duplex with modified nucleotides provide resistance to nucleases. Based on the knowledge available to the person of ordinary skill of the ways to incorporate modified nucleotides (including gapmer structures) and the usefulness of modified nucleotides in providing nuclease stability and binding affinity that is provided by the teachings of Mania [sic] et al, and Baracchini et al., the person of ordinary skill would be motivated to use these known modifications and modification patterns as a starting point for optimizing the stability and affinity of short duplexes.

Id., at 9. It should be noted that the "short duplexes" the examiner proposes to modify is the *hypothetical* duplex the examiner has previously constructed from assorted teachings of Wyatt, Monia and Mancehe.

Lest there be any doubt about the hindsight nature of the pending rejection, one need only consider the examiner's statement that Wyatt, Monia and Manche are relied upon to "demonstrate that synthesis of short duplexes of RNAs for the purpose of studying the activity and structural requirements of different enzymes {sic, was known?}." Examiner's Answer at 11. Clearly, the examiner is not starting with a prior art duplex and modifying that duplex in accordance with factual teachings from the applied references. Rather, the examiner conjures up a hypothetical duplex of unknown composition and then proceeds to modify that hypothetical complex. .35 U.S.C. § 103(a) requires that obviousness requires comparison of the "subject matter sought to be patented" and "the prior art." The examiner's *hypothetical* duplex is just that, *hypothetical*, and is not taught or suggested by the applied prior art.

The Examiner Belatedly Considers Dr. Corey's Declaration

As discussed in the Appeal Brief, the examiner did not consider Dr. Corey's declaration as a rebuttal to the new rejection made when the examiner reopened prosecution in response to appellants' request for a pre-appeal brief conference. Appeal Brief at 14. The examiner states that the Corey declaration was considered in the final office action of March 16, 2011.

Examiner's Answer at 9. That office action has been carefully reviewed again and no mention of Dr. Corey's declaration can be found. Upon reopening prosecution, it was incumbent upon the examiner to consider Dr. Corey's declaration as a rebuttal to the new rejections since it was of record at that time. Appellants relied upon the Corey declaration in responding to the new rejections. Response filed December 16, 2010, at 6-8. The examiner now comments upon the Corey declaration for the first time in responding to the arguments made in Appeal Brief. The examiner's comments are belated and Dr. Corey's declaration stands unrebutted.

Conclusion

For the reasons set forth in the Appeal Brief and those set forth above, it is believed that the examiner's rejections are in error and should be reversed. Such action is earnestly solicited.

No fee is believed to be due in association with the filing of this Reply Brief. If there is a fee due, please charge the amount due to Deposit Account No. 23-3050.

Respectfully submitted,

Date: August 20, 2012

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